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(54) Title: **NOVEL METHODS OF IMAGING AND TREATMENT WITH TARGETED COMPOSITIONS**

(57) Abstract: Novel ultrasound methods comprising administering to a patient a targeted vesicle composition which comprises vesicles comprising a lipid, protein or polymer, encapsulating a gas, in combination with a targeting ligand, and scanning the patient using ultrasound. The scanning may comprise exposing the patient to a first type of ultrasound energy and then interrogating the patient using a second type of ultrasound energy. The targeting ligand preferably targets tissue, cells or receptors, including myocardial cells, endothelial cells, epithelial cells, tumor cells and the glycoprotein GPIIb/IIIa receptor. The methods may be used to detect a thrombus, enhancement of an old or echogenic thrombus low concentrations of vesicles and vesicles targeted to tissues, cells or receptors.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 00/02620

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K49/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

PAJ, WPI Data, EPO-Internal, BIOSIS, MEDLINE, CANCERLIT, EMBASE, DISSERTATION ABS
CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|--|-----------------------|
| X, L | WO 96 40285 A (IMARX PHARMACEUTICAL CORP ; UNGER EVAN C (US); SHEN DEKANG (US); WU) 19 December 1996 (1996-12-19) the whole document L: Priority — -/- | 1-72 |

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
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- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
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Date of the actual completion of the international search

18 October 2000

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22/11/2000

Name and mailing address of the ISA

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INTERNATIONAL SEARCH REPORT

Initial Application No.

PCT/US 00/02620

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|--|-----------------------|
| X | <p>UNGER EVAN C ET AL: "In vitro studies of a new thrombus-specific ultrasound contrast agent." AMERICAN JOURNAL OF CARDIOLOGY, vol. 81, no. 12 SUPPL. A, 12 June 1998 (1998-06-12), pages 58G-61G, XP002087505 & Symposium: Ninth International Congress on Echocardiography: Clinical Cardiology, 1997 ISSN: 0002-9149 abstract page 58G, right-hand column page 59G, right-hand column, paragraph RESULTS page 61G, left-hand column, paragraph DISCUSSION</p> | 1-72 |
| Y | <p>WU YUNQIU ET AL: "Preliminary report: Binding and lysing of blood clots using MRX-408." INVESTIGATIVE RADIOLOGY, vol. 33, no. 12, December 1998 (1998-12), pages 880-885, XP000952676 ISSN: 0020-9996 abstract page 882, left-hand column figure 6 page 884, right-hand column, paragraph DISCUSSION -page 885</p> | 1-72 |
| Y | <p>TAKEUCHI M ET AL: "Enhanced visualization of intravascular thrombus with the use of a thrombus targeting ultrasound contrast agent (MRX408): Evidence from in vivo experimental echocardiographic studies." JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY, vol. 31, no. 2 SUPPL. A, February 1998 (1998-02), page 57A, abstract 803-6 XP000952675 & 47th Annual Scientific Session of the American College of Cardiology; Atlanta, Georgia, USA; March 29-April 1, 1998 ISSN: 0735-1097 abstract</p> | 1-72 |

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INTERNATIONAL SEARCH REPORT

Initial Application No

PCT/US 00/02620

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|--|-----------------------|
| Y | HAUTANEN A ET AL: "Effects of modifications of the RGD sequence and its context on recognition by the fibronectin receptor." JOURNAL OF BIOLOGICAL CHEMISTRY, JAN 25 1989, VOL. 264, NO. 3, PAGE(S) 1437-1442, XP002150374 abstract page 1439, left-hand column, last paragraph -right-hand column, line 15 figure 5 page 1441, right-hand column, line 39 - line 56 — | 1-72 |
| P,X, L | EP 0 901 793 A (IMARX PHARMACEUTICAL CORP) 17 March 1999 (1999-03-17) paragraph '0190! L: Priority example 3 — | 1-72 |
| P,X, L | WO 99 13919 A (IMARX PHARMACEUTICAL CORP) 25 March 1999 (1999-03-25) examples 4,5,10 L: Priority — | 1-72 |

FURTHER INFORMATION CONTINUED FROM PCT/ASA/ 210

Continuation of Box I.2

Claims Nos.: 1-72 in part

Present claims 1-72 relate to a method using an extremely large number of possible compositions. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compositions claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the methods using a composition described in the examples, with special emphasis on examples 60-66.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Int. l. Application No

PCT/US 00/02620

| Patent document cited in search report | Publication date | Patent family member(s) | Publication date |
|---|---------------------|--|--|
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